152. (Amended) The primer oligonucleotide of claim 147, consisting of or contained within a nucleotide base sequence selected from the group consisting of SEQ ID NO: 23, and the fully complementary sequence of the same length thereof.

**Add the following new claims:**

170. **(New)** The composition of claim 80 wherein said probe contains a detectable label.

171. **(New)** The composition of claim 170 wherein said detectable label is an acridinium ester.

172. **(New)** The composition of claim 170 further comprising first and second helper oligonucleotides, wherein the first helper oligonucleotide comprises SEQ ID NO: 9 and the second helper oligonucleotide comprises SEQ ID NO: 10.

Remarks

Applicants thank the Examiner for his careful evaluation of the claims in the previous office action. Responsive to the issues raised by the Examiner, the following comments are provided:

1. With respect to the objection to claims 82, 83, 91, and 156 under 37 C.F.R 1.75(c), Applicants note that the multiple dependency of claims 82 and 91 have been eliminated thereby making the form of the claims come into compliance with statutory requirements of 37 C.F.R. 1.75(c). Further, new claims 170, 171, and 172 have been added keeping the desired dependency of certain of the claims while avoiding overlapping multiple dependencies of the claims. Given the above amendments, Applicants respectfully request that the rejection be withdrawn.

2. With respect to the rejection of claims 50, 51, and 54 under 35 U.S.C. 112, second paragraph, as being indefinite for lack of antecedent basis, Applicants have deleted the phrase "Plurality of" from claims 50, 51 and 54, and also from claims 144-146. Claim 50 now recites the oligonucleotide of claim 40. Claims 50 and 51 now more clearly claim a composition comprising two or more oligonucleotides of claim 40. Claims 144 and 145 now more clearly claim a composition comprising two or more oligonucleotides of claim143. Claims 54 and 146 now claim the composition of claims 51 and 145, respectively. Given these amendments, Applicants respectfully request that the rejection be withdrawn.

3. In order to clarify the priority data so that a more complete enabling support may be found in parent application, the "Related Applications" data of the specification has been amended. Additionally, the title of the patent is amended to more clearly reflect the subject matter of the claimed invention.

4. Regarding the rejection of claims 39, 40, 67, 69, 71-76, 78-80, 84-86, 88-90, 95-99, 101-104, 106-122, 124-143, 147-151, 157-162, and 164-167 under 35 U.S.C. 102(e) as being anticipated by Kacian et al. (p/N 5,554,516), it appears that the Examiner, having provided the office action in May of 2000, quoted old 102(e) language. As Applicant understand the implementation of newly legislated revised 37 C.F.R. § 102(e), inventions that are commonly owned are no longer to be considered prior art under newly revised § 103(c). Since Kacian et al. was owned by the Assignee of record of the current application, Applicants respectfully request that this rejection be withdrawn.

5. Respecting the rejection of claim 98 under 35 U.S.C. 102(e) as being anticipated by Young (P/N 5,422,242), Applicants respectfully traverse this rejection and request the Examiner to withdraw the rejection. Applicants note that notwithstanding the possibility for the complement of Seq. Id. No. 5 of Young to hybridize to the region of *Mycobacterium* nucleic acid sequence denoted by the present Seq. Id. No. 3, the issue to be examined is not the fact that Young discloses Seq. Id. No.5 but rather whether the presently rejected claim as a whole is

disclosed by Young. The present claim 98 claims a "probe" mixture comprising a probe that will hybridize to Seq. Id. No. 3 or its complement and a "helper" probe. Applicants respectfully direct the Examiner's attention to page 16 of the present disclosure wherein is disclosed the nature of a helper probe. Such helper is used for a particular purpose, such as for example, aiding binding of promoter-primer or of a detection probe to target nucleic acid sequence. In contrast, Young does not claim or disclose a probe mix comprising helper probes but rather simply discloses 5' and 3' primers for amplification (as in claim 8) and probes for detection of amplified sequences (such as those claimed in claim 10). (See Young columns 7 and 8). Moreover, Young claims a kit having such primers and such detection probes. Such kits do not involve "helper" probes and nowhere does Young even mention helper probes. In any event, the combination of primer and detection probes is not the equivalent of the presently claimed "probe" mix. Therefore, it is improper to combine Young's claims 8 and 10 to derive at Applicant's claim 98. Consequently, Applicants submit that the necessary elements for anticipation under 35 U.S.C. 102(e) are absent, and Applicants respectfully request the rejection to be withdrawn.

6. The Examiner has rejected claims 74, 75, 147-149, and 152 under 35 U.S.C. 102 (e) as being anticipated by Shah (P/N 5,521,300) alleging that sequence number 48 in Shah et al anticipates the above listed instant claims due to its hybridization limitations. Applicants respectfully direct the Examiner's attention to the above amendments to the claims which render the Examiner's rejection moot. Thus, Applicants request that the rejection be withdrawn.

7. Respecting the rejection of claims 39-42, 48-51, 54-56, 67-69, 71-76, 78-80, 84-86, 88-90, 92, 93, 95-99, 101-104, 106-122, 124-155, and 157-169 under 35 U.S.C. 103(a) over Kacian (P/N 5,554,516), Applicants respectfully direct the Examiner's attention to the fact that under newly amended 103, as stated above, Kacian is not a valid prior art reference. Thus, Applicants respectfully traverse this rejection and request it be withdrawn.

8. Finally, respecting the Hammond reference, Applicants understand that although the

reference disclose the sequences SEQ ID Nos 8-10, such sequences are not claimed in the manner presently used in the instant claims. Therefore, there is not an objectionable issue to be addressed with respect to this reference.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Given the above amendments and remarks, Applicants believe the application is now in condition for allowance. No fee is believe due respecting the instant response, however, if any fee is due please charge our deposit account Number 50/1273 in the appropriate amount. If the Examiner needs to reach me, my direct telephone number is (858) 720-2757.

Respectfully submitted,
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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the specification:**

1. Title change:

[NUCLEIC ACID SEQUENCE AMPLIFICATION] --Oligonucleotides for Nucleic Acid Amplification and for the Detection of *Mycobacterium tuberculosis* –

2. Change in related applications:

[This application is a continuation-in-part of Kacian et al., U.S. Serial Nos.: 07,855,732, filed March 19, 1992, 07/550,837, filed July 10, 1990, and 07/379,501, filed July 11, 1989, all hereby incorporated by reference herein.]

--This application is a divisional of U.S. Application Serial No. 08/345,861, filed November 28, 1994, which is a continuation of U.S. Application Serial No. 07/925,405, filed August 4, 1992, now abandoned.—

**In the claims:**

1. Claim 74 is cancelled without prejudice to its future prosecution.

2. Claims amended:

50. (Twice amended) [The plurality of] An oligonucleotide[s] of claim 40, wherein [one or more of] said oligonucleotide[s] is modified at its 3' end to reduce or block extension [of said one or more] of said oligonucleotide[s] by a polymerase.

51. (Three times amended) A composition comprising two or more [plurality of] oligonucleotides of claim 40, wherein one or more of said oligonucleotides is unmodified at the 3' end and one or more of said oligonucleotides is modified at the 3' end to reduce or block extension by a polymerase.

54. (Three times amended) The composition [plurality of oligonucleotides] of claim 51, wherein one or more of said oligonucleotides is differently modified at the 3' end to reduce or block extension by a polymerase.

75. (Twice amended) [The] A composition [of claim 74] for amplification of *Mycobacterium tuberculosis* nucleic acid comprising [two or more of said] first and a second primer oligonucleotides, wherein said first primer consists of the primer oligonucleotide of claim 147, and said second primer consists of an oligonucleotide from about 10 to about 100 nucleotide bases in length which will, under nucleic acid amplification conditions, hybridize to a region of *Mycobacterium tuberculosis* nucleic acid selected from the group consisting of SEQ ID NO: 7 and its complement.

76. (Twice amended) The composition of claim [74] 75 wherein said [comprising a] first primer oligonucleotide [which] comprises a nucleotide base sequence selected from the group consisting of SEQ ID NO: 23 and [SEQ ID NO: 7] its complement.

77. (Twice amended) The composition of claim 76 [further comprising a] wherein said second primer oligonucleotide [which] comprises a nucleotide base sequence [different from that of the first primer oligonucleotide, wherein the nucleotide base sequence of the second primer oligonucleotide is] selected from the group consisting of [SEQ ID NO: 23 and] SEQ ID NO: 7 and its complement.

78. (Twice amended) The composition of any one of claims [74,] 75, [or] 76, or 77, wherein one or more primer oligonucleotides further comprises, in the 5' upstream region, a nucleotide base sequence which is recognized by an RNA polymerase and which enhances transcription initiation or polymerization by said RNA polymerase.

79. (Three times amended) The composition of any one of claims [74] 75, 76, or 77, further comprising a nucleic acid hybridization assay probe from about 10 to about 100 nucleotide bases in length which will hybridize with at least 10 contiguous bases of a nucleotide base sequence region of *Mycobacterium tuberculosis* nucleic acid to form a detectable duplex under hybridization conditions, wherein said region is selected from the group consisting of SEQ ID NO: 8 and the perfectly complementary sequence thereto.

82. (Twice amended) The composition of claim 79 [or 80] wherein said probe contains a detectable label.

91. (Amended three times) The composition of claim 89 [or 90], wherein said probe comprises an oligonucleotide selected from the group consisting of SEQ ID NO: 3 and the perfectly complementary sequence thereto.

143. (Amended) An oligonucleotide of about 20 to about 100 bases in length [comprising] consisting of a nucleic acid sequence selected from the group consisting of xCCAGGCCACTTCCGCTAACC (SEQ ID: 6 or 23), xCGCGGAACAGGCTAAACCGCACGC (SEQ ID: 7), and their fully complementary sequences of the same length, wherein x is nothing or is a sequence recognized by an RNA polymerase.

144. (Amended) A composition comprising two or more[The plurality of] oligonucleotides of claim 143, wherein one or more of said oligonucleotides is modified at the 3' end to reduce or block extension of said one or more of said oligonucleotides by a polymerase.

145. (Amended) A composition comprising two or more [plurality of] oligonucleotides of claim 143, wherein one or more of said oligonucleotides is unmodified at the 3' end and one or more of said oligonucleotides is modified at the 3' end to reduce or block extension by a polymerase.

146. (Amended) The [plurality of oligonucleotides] composition of claim 145, wherein one or more of said oligonucleotides is differently modified at the 3' end to reduce or block extension by a polymerase.

147. (Amended) A primer oligonucleotide from 10 to 100 nucleotide bases in length

able to hybridize to a region of *Mycobacterium tuberculosis* nucleic acid, wherein said region consists of a nucleotide base sequence selected from the group consisting of [SEQ ID NO: 7,] SEQ ID NO: 23, and [their] the fully complementary sequence[s] of the same length thereof.

151. (Amended) The primer oligonucleotide of claim 147, comprising a nucleotide base sequence selected from the group consisting of [SEQ ID NO: 7,] SEQ ID NO: 23, and [their] the fully complementary sequence[s] of the same length thereof.

152. (Amended) The primer oligonucleotide of claim 147, consisting of or contained within a nucleotide base sequence selected from the group consisting of [SEQ ID NO: 7,] SEQ ID NO: 23, and [their] the fully complementary sequence[s] of the same length thereof.

3. Newly added claims:

170. **(New)** The composition of claim 80 wherein said probe contains a detectable label.

171. **(New)** The composition of claim 170 wherein said detectable label is an acridinium ester.

172. **(New)** The composition of claim 170 further comprising first and second helper oligonucleotides, wherein the first helper oligonucleotide comprises SEQ ID NO: 9 and the second helper oligonucleotide comprises SEQ ID NO: 10.